

Clinical Policy: Doxycycline (Doryx, Oracea)
Reference Number: CP.PMN.##
Effective Date: XX/XX
Last Review Date: 05/17
Line of Business: Medicaid

[Coding Implications](#)
[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Doxycycline (Doryx[®], Doryx[®] MPC, Oracea[®]) is a tetracycline-class drug.

FDA approved indication

Doryx/Doryx MPC is indicated for

- Rickettsial infections
- Sexually transmitted infections
- Respiratory tract infections
- Specific bacterial infections
- Ophthalmic infections
- Anthrax, including inhalational anthrax (post-exposure)
- Alternative treatment for selected infections when penicillin is contraindicated
- Adjunctive therapy in acute intestinal amebiasis and severe acne
- Prophylaxis of malaria

Oracea is indicated for the treatment of only inflammatory lesions (papules and pustules) of rosacea in adult patients. No meaningful effect was demonstrated for generalized erythema (redness) of rosacea.

Limitations of Use: This formulation of doxycycline has not been evaluated in the treatment or prevention of infections. Oracea should not be used for treating bacterial infections, providing antibacterial prophylaxis, or reducing the numbers or eliminating microorganisms associated with any bacterial disease. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, Oracea should be used only as indicated. Efficacy of Oracea beyond 16 weeks and safety beyond 9 months have not been established. Oracea has not been evaluated for the treatment of the erythematous, telangiectatic, or ocular components of rosacea.

Policy/Criteria

Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Centene Corporation[®] that Doryx, Doryx MPC, or Oracea is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Rosacea (must meet all):

1. Diagnosis of rosacea with inflammatory lesions (papules and pustules);

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2. Request is for Oracea;
3. Failure of ≥ 4 week trial of topical metronidazole, unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of ≥ 4 week trial of topical sulfacetamide sodium with sulfur, unless contraindicated or clinically significant adverse effects are experienced;
5. Member experienced clinically significant adverse effects to immediate-release doxycycline or has contraindication(s) to the excipients in immediate-release doxycycline;
6. Failure of two PDL oral tetracycline antibiotics, each trialed for ≥ 4 weeks, unless clinically significant adverse effects are experienced; Failure of ≥ 4 week trial of one additional PDL oral tetracycline antibiotic, unless clinically significant adverse effects are experienced;
- ~~5.~~
- ~~6-7.~~ No documentation of hypersensitivity to tetracyclines;
- ~~7-8.~~ Dose does not exceed 40 mg/day (1 capsule/day).

Approval duration: 16 weeks

B. Acne Vulgaris (must meet all):

1. Diagnosis of acne vulgaris;
2. Request is for Doryx or Doryx MPC;
3. Failure of two PDL topical antibiotics for acne, each trialed for ≥ 4 weeks, unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of ≥ 4 week trial of one PDL topical tretinoin unless contraindicated or clinically significant adverse effects are experienced (Note: prior authorization may be required);
5. Member experienced clinically significant adverse effects to immediate-release doxycycline or has contraindication(s) to the excipients in immediate-release doxycycline;
6. Failure of ≥ 4 week trial of one additional PDL oral tetracycline antibiotic, unless clinically significant adverse effects are experienced;
- ~~5.~~ Failure of two PDL oral tetracycline antibiotics, each trialed for ≥ 4 weeks, unless clinically significant adverse effects are experienced;
- ~~6-7.~~ No documentation of hypersensitivity to tetracyclines.

Approval duration: 3 months

C. Prophylaxis of Malaria (must meet all):

1. Prescribed for malaria prophylaxis;
2. Request is for Doryx or Doryx MPC;
3. Member experienced clinically significant adverse effects to immediate-release doxycycline or has contraindication(s) to the excipients in immediate-release doxycycline;
4. No documentation of hypersensitivity to tetracyclines;
5. Dose does not exceed 100 mg per day (Doryx) or 120 mg per day (Doryx MPC).

Approval duration: 4 months or duration of travel and up to 4 weeks after member leaves the malarious area (whichever is less)

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D. Other FDA Approved Indications for Doryx/Doryx MPC (must meet all):

1. Prescribed for the treatment of one of the following conditions or diseases (refer to Appendix B for conditions or diseases that are applicable):
 - a. Rickettsial infections;
 - b. Sexually transmitted infections;
 - c. Respiratory tract infections;
 - d. Specific bacterial infections;
 - e. Ophthalmic infections;
 - f. Anthrax, including inhalational anthrax (post-exposure);
 - g. Selected infections when penicillin is contraindicated;
 - h. Acute intestinal amebiasis;
2. Request is for Doryx or Doryx MPC;
3. Member experienced clinically significant adverse effects to immediate-release doxycycline or has contraindication(s) to the excipients in immediate release doxycycline;
4. Failure of one additional PDL oral tetracycline antibiotic, unless clinically significant adverse effects are experienced *or* the other PDL tetracycline antibiotics are not indicated for the member's diagnosis;
- ~~3. Failure of two PDL tetracycline antibiotics, unless clinically significant adverse effects are experienced *or* PDL tetracycline antibiotics are not indicated for the member's diagnosis;~~
- ~~4.5.~~No documentation of hypersensitivity to tetracyclines.

Approval duration: 60 days or duration of request (whichever is less)

E. Other diagnoses/indications

1. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Rosacea (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Request is for Oracea;
3. Documentation of positive response to therapy;
4. Member has not received Oracea daily for ≥ 16 weeks;
5. Dose does not exceed 40 mg/day (1 capsule/day).

Approval duration: up to 16 weeks of treatment (total)

B. Acne Vulgaris (must meet all):

1. Request is for Doryx/Doryx MPC;
2. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
3. Documentation of positive response to therapy.

Approval duration: 3 months

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C. Other Indications for ~~Doryx/Doryx MPC~~, Acute Infections and including Malaria Prophylaxis (must meet all):

1. Therapy for Doryx/Doryx MPC may not be renewed. Member must meet initial approval criteria for approval of Doryx/Doryx MPC.

Approval duration: N/A

D. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

Approval duration: 3 months or duration of request (whichever is less)

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

PDL: preferred drug list

N/A: not applicable

Appendix B: Other FDA Approved Indications for Doryx/Doryx MPC

FDA approved indications	Applicable conditions or diseases
Rickettsial infections	Rocky Mountain spotted fever, typhus fever and the typhus group, Q fever, rickettsialpox, and tick fevers caused by Rickettsiae
Sexually transmitted infections	Uncomplicated urethral, endocervical or rectal infections caused by Chlamydia trachomatis Nongonococcal urethritis caused by Ureaplasma urealyticum Lymphogranuloma venereum caused by Chlamydia trachomatis Granuloma inguinale caused by Klebsiella granulomatis Uncomplicated gonorrhea caused by Neisseria gonorrhoeae Chancroid caused by Haemophilus ducreyi.
Respiratory tract infections	Respiratory tract infections caused by Mycoplasma pneumoniae Psittacosis (ornithosis) caused by Chlamydochila psittaci Doxycycline is indicated for treatment of infections caused by the following micro-organisms, when bacteriological testing indicates appropriate susceptibility to the drug: Respiratory tract infections caused by Haemophilus influenzae Respiratory tract infections caused by Klebsiella species Upper respiratory infections caused by Streptococcus pneumoniae

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Specific bacterial infections	<p>Relapsing fever due to <i>Borrelia recurrentis</i> Plague due to <i>Yersinia pestis</i> Tularemia due to <i>Francisella tularensis</i> Cholera caused by <i>Vibrio cholerae</i> <i>Campylobacter fetus</i> infections caused by <i>Campylobacter fetus</i> Brucellosis due to <i>Brucella</i> species (in conjunction with streptomycin) Bartonellosis due to <i>Bartonella bacilliformis</i></p> <p>Doxycycline is indicated for treatment of infections caused by the following gram- negative microorganisms, when bacteriological testing indicates appropriate susceptibility to the drug: <i>Escherichia coli</i>, <i>Enterobacter aerogenes</i>, <i>Shigella</i> species, <i>Acinetobacter</i> species, urinary tract infections caused by <i>Klebsiella</i> species</p>
Ophthalmic infections	<p>Trachoma caused by <i>Chlamydia trachomatis</i> Inclusion conjunctivitis caused by <i>Chlamydia trachomatis</i></p>
Anthrax including inhalational anthrax (post-exposure)	Anthrax due to <i>Bacillus anthracis</i> , including inhalational anthrax (post-exposure)
Alternative treatment for selected infections when penicillin is contraindicated	<p>Syphilis caused by <i>Treponema pallidum</i> Yaws caused by <i>Treponema pallidum</i> subspecies <i>pertenue</i> Vincent’s infection caused by <i>Fusobacterium fusiforme</i> Actinomycosis caused by <i>Actinomyces israelii</i> Infections caused by <i>Clostridium</i> species</p>
Adjunctive therapy for acute intestinal amebiasis	N/A

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Acne vulgaris and other FDA approved indications	<p><u>Doryx</u></p> <p><i>Adults:</i> The usual dose of oral doxycycline is 200 mg on the first day of treatment (administered 100 mg every 12 hours), followed by a maintenance dose of 100 mg daily. The maintenance dose may be administered as a single dose or as 50 mg every 12 hours. In the management of more severe infections (particularly chronic infections of the urinary tract), 100 mg every 12 hours is recommended.</p> <p><i>For pediatric patients above eight years of age:</i> The recommended dosage schedule for children weighing 45 kg or less is 4.4 mg/kg of body weight divided into two doses on the first day of treatment, followed by 2.2 mg/kg of body weight given as a single daily dose or</p>	Based on weight and indication.

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	<p>divided into two doses on subsequent days. For more severe infections up to 4.4 mg/kg of body weight may be used. For children over 45 kg, the usual adult dose should be used</p> <p><u>Doryx MPC</u> <i>Adults:</i> The usual dosage is 240 mg on the first day of treatment (administered 120 mg every 12 hours) followed by a maintenance dose of 120 mg daily. In the management of more severe infections (particularly chronic infections of the urinary tract), 120 mg every 12 hours is recommended. <i>Pediatrics:</i> For all pediatric patients weighing less than 45 kg with severe or life threatening infections (e.g., anthrax, Rocky Mountain spotted fever), the recommended dosage is 2.6 mg per kg of body weight administered every 12 hours. Pediatric patients weighing 45 kg or more should receive the adult dose. For pediatric patients with less severe disease (greater than 8 years of age and weighing less than 45 kg), the recommended dosage schedule is 5.3 mg per kg of body weight divided into two doses on the first day of treatment, followed by a maintenance dose of 2.6 mg per kg of body weight (given as a single daily dose or divided into twice daily doses). For pediatric patients weighing over 45 kg, the usual adult dose should be used.</p> <p>See Full Prescribing Information for additional indication specific dosage information</p>	
Malaria prophylaxis	<p><u>Doryx</u> <i>Adults:</i> The recommended dose is 100 mg daily. <i>For children over 8 years of age:</i> The recommended dose is 2 mg/kg given once daily up to the adult dose.</p> <p><u>Doryx MPC</u> <i>Adults:</i> The recommended dose is 120 mg daily. <i>For pediatric patients 8 years of age and older:</i> The recommended dosage is 2.4 mg per kg of body weight administered once daily. <i>Pediatric patients weighing 45 kg or more:</i> should receive the adult dose.</p> <p>Prophylaxis should begin 1 or 2 days before travel to the malarious area. Prophylaxis should be continued</p>	<p><u>Doryx</u> 100 mg/day</p> <p><u>Doryx MPC</u> Adults, adolescents, and children 8 years and older weighing 45 kg or more: 120 mg/day</p> <p>Children 8 years and older and adolescents</p>

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	daily during travel in the malarious area and for 4 weeks after the traveler leaves the malarious area.	weighing less than 45 kg: 2.4 mg/kg/dose/day
Rosacea	<u>Oracea</u> Adults: 40 mg orally once daily	40 mg/day

VI. Product Availability

Drug	Availability
Doryx	Delayed-release tablets: 50 mg, 200 mg
Doryx MPC	Delayed-release tablets: 120 mg
Oracea	Capsules: 40 mg

VII. Workflow Document



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Field Code Changed

VIII. References

1. Oracea Prescribing Information. Fort Worth, TX: Galderma Laboratories, L.P.; December 2014. Available at: www.oracea.com. Accessed January 11, 2017.
2. Doryx Prescribing Information. Greenville, NC: Mayne Pharma; July 2015. Available at: www.doryx.com. Accessed January 11, 2017.
3. Oge LK, Muncie HL, Phillips-Savoy AR. Rosacea: Diagnosis and Treatment. Am Fam Physician. 2015;92(3):187-196.
4. Del Rosso JQ, Thiboutot D, Gallo R. Consensus Recommendations from the American Acne & Rosacea Society on the Management of Rosacea, Part 5: A Guide on the Management of Rosacea. Cutis. 2014 March;93(3):134-138.
5. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol. 2016;74(5):945-973.
6. Arguin PM, Tan KR. Chapter 3. Infectious diseases related to travel. Malaria. In: Centers for Disease Control and Prevention. 2014 Yellow Book - Traveler's Health. Atlanta: U.S. Department of Health and Human Services, Public Health Service. 2014. Available at: <http://wwwnc.cdc.gov/travel/yellowbook/2014/chapter-3-infectious-diseases-related-to-travel/malaria>.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PMN.51 Tetracycline Antibiotics (Solodyn, Doryx, Oracea) to address all indications for the featured drugs Clinical changes made to criteria:	03 /17	<u>05/17</u>

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
<p>-For acne vulgaris and rosacea, modified criteria related to trial and failure of PDL oral antibiotics to specifically require tetracycline class of antibiotics, <u>one of which must be immediate-release doxycycline</u>, as they are considered first-line for systemic antibiotic therapy; for rosacea, modified criteria to require failure of 2 (instead of 1) oral antibiotics;</p> <p>-Created criteria sets for other FDA approved indications of Doryx, including malaria prophylaxis</p> <p>Non-clinical changes to criteria:</p> <p>-Converted to new template</p> <p>-Added no documentation of hypersensitivity to tetracyclines per PI</p> <p>-Added duration of trial to requirements related to trial and failure of topical therapies for clarity</p> <p>-Removed age requirement since tetracycline antibiotics on the PDL are not subjected to age restrictions</p> <p>-For acne, modified duration of trial of oral antibiotics from ≥ 6 weeks to ≥ 4 weeks; modified duration of approval for Doryx/Doryx MPC from 16 weeks to 12 weeks since PI does not specify time frame of use and per American Academy of Dermatology, systemic antibiotic use should be limited to shortest possible duration, typically 3 months, to minimize development of bacterial resistance</p> <p>-Updated references</p>		

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does

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not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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